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10/764,330	01/23/2004	Michael P. Cooke	P1097US10	5772

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EXAMINER	
JUEDES, AMY E	

ART UNIT	PAPER NUMBER
1644	

DATE MAILED: 12/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/764,330	COOKE ET AL.	
	Examiner	Art Unit	
	Amy E. Juedes, Ph.D.	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 September 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-27* is/are pending in the application.

4a) Of the above claim(s) *7 and 17-27* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-6 and 8-16* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's amendment, filed 9/22/06, is acknowledged.

Claim 13 has been amended.
Claims 1-27 are pending.

2. Applicant's election with traverse of group I, drawn a method for identifying an agent, claims 1-16, in the reply filed on 9/22/06 is acknowledged. Applicant has further elected accession No. NP_002212 as the species of IP3K.

Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 17-27 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention. Claim 7 is withdrawn as being drawn to a non-elected species.

Claims 1-6 and 8-16 read on the elected invention and are being acted upon.

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) The term "modulates" is a relative term that renders claims 1, 2, 4, 9, 11-12, 14, and 16 indefinite. The specification on page 9 states that the term "modulate" with respect to IP3K refers to a change in the cellular level or other biological activities of IP3K. However, this definition is not adequate to define the metes and bounds of term "modulates". For example, it is not at all clear what "other biological activities" might encompass. Additionally, it is not

clear what direction, degree, or type of modulation is required. For example "modulates" might encompass an increase or a decrease in activity. Additionally, modulate might indicate that an activity is turned on or off, or could also indicate an upregulation or downregulation of a particular activity to an unspecified degree. In addition, said modulation could be intermittent, or constant. Therefore, even taking into account the definition provided by the instant specification, the term modulates is so vague that the metes and bounds of the claims cannot be established. Furthermore, it is noted that no definition is provided as to the metes and bounds of "modulating" T cell lymphocyte development or function, as recited in claim 1.

B) Claims 4, 8, and 14-15 are indefinite in the recitation of a method wherein the modulating agent inhibits kinase activity. The claims do not actually recite an active method step, and it is unclear how the inhibition of kinase activity relates to independent claim 1, which comprises identifying an IP3K modulating agent. Are the claims intended to mean that the cellular activity being assaying for in claim 1 is kinase activity?

C) Claims 9-11 are indefinite, in the recitation of a modulating agent that decreases cellular levels of IP3K, or inhibits expression of the gene encoding IP3K. It is unclear how the ability to inhibit gene expression is related to the method of independent claim 1. Are the claims intended to mean that the identified modulatory agents that inhibit cellular activity (for example, kinase activity), are also capable of inhibiting IK3K gene expression by some type of feedback mechanism? Or are the claim intended to mean that the cellular activity being assaying for in claim 1 is the cellular level of IP3K? If the latter, it is unclear how the cellular level of IP3K gene can be considered a "cellular activity" of IP3K.

D) Claim 11 is indefinite in the recitation of a method wherein the modulating agent inhibits expression of a gene encoding IP3K. The claims do not actually recite an active method step, and it is unclear how the inhibition of gene expression relates to independent claim 1, which comprises identifying an IP3K modulating agent. Are the claims intended to mean that the assay for cellular activity in claim 1 comprises measuring gene expression?

5. Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The claims are incomplete for omitting essential steps. While all of the technical details need not be recited, the claims should include enough information to clearly and accurately describe the invention and how it is to be practiced. The instant claims are drawn to a method comprising assaying a cellular activity of IP3K in the presence of a test compound to identify a modulating agent. However, the instant claims do not specify how the modulating is to be identified. For example, is the test compound identified as a modulating agent if it exhibits a particular effect on the IP3K, or is the modulatory agent some other component of the assay? Additionally, the instant claims are drawn to a method of identifying an agent that modulates T lymphocytes, but the resolution step recites identification of an agent that modulates IP3K. Thus, the instant claims lack a correlation step describing how the claimed method results in the identification of an agent that modulates T lymphocytes.

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Specifically, there is insufficient written description to show that Applicant was in possession of the genus of molecules encompassed by "IP3K", "fragments" of IP3K, or a "substantially identical" IP3KB.

The instant claims encompass assaying a cellular activity of an "IP3K". "IP3K" encompasses broad genus of different kinases. For example, IP3K exists as several isoforms including IP3K A, B, and C. Furthermore, "IP3K" encompasses kinases derived from any species, for example, mouse, human, rat, horse,

dog, monkey, etc. Furthermore, the claims might encompass splice variants or polymorphic IP3 kinases. These IP3K kinases are all structurally different due to their unique amino acid sequences. In contrast to the broad genus of kinases encompassed by the claims, Applicant has only disclosed IP3K kinases from mouse, human, or rat.

Additionally, "fragments" of IP3K represents an extremely large genus of proteins. It is noted that neither the claims nor the specification define any functional limitations for said fragments. For example the claims might even encompass assaying a cellular activity of short peptides of IP3K. Therefore, "fragments" of IP3K might encompass a virtually unlimited number of structurally (i.e. comprising a unique amino acid sequence) different proteins. Additionally, Applicant has not disclosed a single species of "fragment".

Additionally, methods using proteins "substantially identical" to the IP3KB amino acid sequences of claim 6 encompass using a broad genus of different proteins. The instant specification on page 8 defines "substantially identical" to be sequences at least 90% identical. Thus, the claims might encompass using proteins with a large number of amino acid substitutions, deletions, or additions to the amino acid sequences of claim 6. The "substantially identical" proteins would all be structurally different due to their unique amino acid sequences. Furthermore, the claims do not recite any functional limitations of the "substantially identical" proteins. Therefore, the instant claims might encompass using structurally different proteins with different cellular activities (i.e. functions). Additionally, Applicant has not disclosed a single species of protein "substantially identical" to the amino acids sequences recited in claim 6. Thus, one of skill in the art would conclude that the specification fails to provide adequate written description to demonstrate that Applicant was in possession of the claimed genus. See *Eli Lilly*, 119 F. 3d 1559, 43, USPQ2d 1398.

8. Claims 1-6 and 8-16 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. Specifically, the specification provides insufficient evidence that the claimed

method would function as a method for identifying an agent that modulates T lymphocytes, as broadly claimed.

The specification disclosure is insufficient to enable one skilled in the art to practice the invention as claimed without an undue amount of experimentation. Undue experimentation must be considered in light of factors including: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill in the art, the level of predictability of the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention, see *In re Wands*, 858 F.2d at 737, 8 USPQ2d at 1404 (Fed. Cir. 1988).

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. With these teachings in mind, an enabling disclosure, commensurate in scope with the breadth of the claimed invention, is required.

With regards to the instant claims, their breadth comprises a primary issue as regards the unpredictability of the claimed method. The instant claims are drawn to a method of identifying an agent that modulates T lymphocytes. The only active step of the claimed method involves assaying a cellular activity of IP3K in the presence of a test compound. The resolution step of the method involves identifying a modulating agent that modulates the cellular activity of the IP3K. However, the claims do not recite how the ability to modulate IP3K correlates with the ability to modulate T cells. It is known that mice deficient in IP3KB have impaired T cell development (see Poullon et al.).

Therefore, it is possible that agents that inhibit IP3KB kinase activity might act as inhibitors of T lymphocyte development. However, the instant claims might encompass identifying an agent that downmodulates IP3K activity as an agent capable of enhancing (i.e. modulating) T cell development or function.

Furthermore, the instant claims encompass assaying any IP3K. IP3K exists as three isoforms that are characterized by unique sequences, tissue distribution, and functions (see Pouillon et al, page 1136). The isoforms are structurally distinct, for example the catalytic domain of IP3 kinase A is only 68% identical with that of IP3 kinase B (see Vanweyenberg et al.). Therefore, agents identified by their ability to modulate IP3KA would not necessarily act as modulators of other IP3 kinases, due to the substantial differences in the structures of their catalytic domains. Furthermore, not all IP3 kinases are even expressed in T cells. For example, IP3KA is expressed exclusively in specific neuronal subpopulations (see Pouillon et al, page 1136). It is unclear how an agent that modulates the activity of IP3KA could be a T cell modulatory agent, since IP3KA is not expressed in T cells. Additionally, the instant claims encompass assaying the "cellular activity" of any IP3K fragment. This might encompass assaying the activity of small peptide fragments to act as antigens (i.e. a "cellular activity"). It is not clear how said assay would be useful for identifying agents that modulate T cell development. Thus, given the state of the art, the instant specification must provide a sufficient and enabling disclosure, commensurate in scope with the instant claims. However, the only data provided by the instant specification demonstrate that IP3KB deficient mice have impaired T cell development. Accordingly, the method as broadly claimed must be considered highly unpredictable. Given said unpredictability, the method of the instant claims must be considered to require undue experimentation.

9. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless -

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

10. Claims 1, 3-4, 6, 8-11 are rejected under 35 U.S.C. 102(a) as being anticipated by Chang et al., 2002 (of record), as evidenced by Wen et al., 2004.

Chang et al. teach a method comprising assaying for the kinase activity of IP3K in the presence of test compounds and identifying compounds that inhibit the activity of IP3K (i.e. a modulatory agent). Furthermore, Chang et al. specifically teach assaying the ability of the kinase to catalyze IP3 to IP4 (see page 900, in particular). Furthermore, since the catalysis of IP3 to IP4 is an activity of IPKB (see Wen et al.), Chang et al. have assayed a cellular activity of IP3KB (including accession NO. NP_002212), as recited in the instant claims. Therefore, since Chang et al. have performed all the steps of the claimed method, the compounds identified by Chen et al. would inherently be able to modulate T lymphocyte development or function or decrease the cellular levels of IP3K gene.

Thus, the reference clearly anticipates the invention.

11. Claims 1-4, 6, 8-15 are rejected under 35 U.S.C. 102(b) as being anticipated by da Silva et al., 1994, as evidenced by Wen et al., 2004.

da Silva et al. teach a method comprising assaying the kinase ability of inositol 1,4,5-triphosphate 3-kinase (i.e. IP3K) in the present of adriamycin (i.e. a test compound), see page 12523, in particular). Furthermore, da Silva et al. specifically teach assaying for the catalysis of IP3 to IP4 (see page 12523 and Fig. 5 in particular). Furthermore, since one activity of IP3KB is converting IP3 to IP4 (see Wen et al., page 5604), da Silva et al. have assayed for a cellular activity of IP3KB (including accession No. NP_002212). da Silva et al. further teach that adriamycin is an agent that inhibits T cell proliferation (i.e. modulates T cell function/differentiation), see Fig. 3 in particular).

Thus, the reference clearly anticipates the invention.

12. No claim is allowed. Claims 5 and 16 are free of the art.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy E. Juedes, Ph.D. whose telephone number is 571-272-4471. The examiner can normally be reached on 8am - 5pm, Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on 571-272-0841. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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11/29/06
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